16. (Amended) A method for comparing two or more lesions in a patient having a neoplastic T-cell disease, comprising:

obtaining a sample from a first lesion and a second lesion in said patient;

determining whether identical clonal TCR gene rearrangements are present in each of said samples by analyzing each of said samples by the method of claim 1 and comparing the results obtains from said analyses.

REMARKS

1. **Claims 1-5, 7, and 9-15 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Menke in view of Chen.**

This rejection is respectfully traversed. The present invention and cited references refer to three separate techniques, Temporal Temperature Gradient Electrophoresis (TTGE, "Method 1"), Temperature Gradient Gel Electrophoresis (TGGE, "Method 2"), and Denaturing Gradient Gel Electrophoresis (DGGE, "Method 3"). The present invention claims a method for determining the clonality of a T-cell receptor (TCR) rearrangement in a sample. The method involves extracting nucleic acid from a sample, amplifying it by PCR, and analyzing the TCR DNA fragments using Method 1.

Menke is the primary reference cited and discloses the use of Method 2 in the analysis of PCR products of TCR rearrangements. Chen discloses the use of Method 1 in the analysis of mitochondrial DNA. The Examiner asserts that it would be obvious to substitute Method 1 disclosed by Chen for Method 2 in Menke to arrive at the present invention.

A prima facie finding of obviousness requires 1) a suggestion or motivation to modify or combine the references; 2) a reasonable expectation of success; and 3) the prior

art references must teach or suggest all the claim limitations (MPEP 2143). In the present case, no motivation is provided to combine Menke with Chen and no reasonable expectation of success is found based on the prior art.

The prior art must be considered in its entirety (MPEP 2141.02). Other references in the art indicate that Method 1 may not be effective for separating particular sequence types. For example, Farnleitner et al. report that Method 1 was unable to separate particular sequence types of *E. coli uidA* amplicons, which could only be separated by Method 3 (Farnleitner, p. 430, Col. 1). Therefore, the person of ordinary skill would acknowledge that there is no reasonable expectation of success that Method 1 will function in analyzing the clonality of T-cell rearrangements. The art provides, at best, a mere invitation to experiment with all methods of electrophoresis in the hopes of identifying a method useful in the analysis of the clonality of T-cell receptor rearrangements.

The expectation of success that Method 1 will function in the determination of the clonality of TCR rearrangements is not found in the prior art, but only with reference to the Applicants' own disclosure. But this is an impermissible use of hindsight that uses the inventors' own success as evidence that the success would have been expected. *In re Kotzab*, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) *quoted approvingly by Life Technologies, Inc. v. Clontech Laboratories, Inc.* 56 USPQ2d 1186 (Fed. Cir. 2000).

In other rejections the Examiner combines Theodorou and Chott with Menke and Chen. But for the same reasons discussed above, no motivation is provided to make the asserted combinations. Nor does the addition of these references cure the deficiencies noted above.

Reconsideration and withdrawal of the rejections is respectfully requested.

Conclusion

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

After amending the claims as set forth above, claims 1-18 are now pending in this application.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date April 21, 2003

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MARKED UP VERSION SHOWING CHANGES MADE

16. (Amended) A method for comparing two or more lesions in a patient having a neoplastic T-cell disease, comprising:

obtaining a sample from a first lesion and a second lesion in said patient;

determining whether identical clonal TCR gene rearrangements are present in each of said samples by analyzing each of said samples by the method of claim 1 and comparing the results obtains from **[sad]** said analyses.